PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/DK2004/000822	26.11.2004	28.11.2003

International Patent Classification (IPC) or both national classification and IPC
C12N15/82, A01N65/00, C07K16/16

Applicant
UNIVERSITY OF COPENHAGEN

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 19-22

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 19-22

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
☐ has not been furnished
☐ does not comply with the standard

the computer readable form
☐ has not been furnished
☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-18,23-26

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	23,25
	No:	Claims	1-18,24,26
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-18,23-26
Industrial applicability (IA)	Yes:	Claims	1-18,23-26
	No:	Claims	

2. Citations and explanations

   see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

1 The following documents are relevant, the numbering will be maintained

D1: EP1033405.
D2: WO0141556.
D3: The Plant Journal 32:975-983, 2002.
D4: bk3western03.pdf, July 1, 2003.
D5: Trends in Plant Science 6(9):392-394, 2001.

Re Item I
Basis of the report

2 **Essentially Biological Process**

2.1 Claims 15,17, and 25 extend to methods within the meaning of Rule 67.1(ii) PCT

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

3 The application lacks unity of invention (cf. Item IV). Additional search fees have not been paid consequently the subject matter relating to claimed invention 2 as defined in claims 19-22 has not been examined.

Re Item IV

Lack of unity of invention

4 The application relates in general to transgenic plants comprising a transgene encoding a MAP kinase substrate 1 (MKS1) polypeptide, one example of which is given by the polypeptide with SEQ ID NO:2. D1 (cf. SEQ ID NO:49382; claims) discloses a polypeptide with the same sequence and transgenic plants comprising it. D2 (cf. claims 1-37) discloses use of MAP kinase sequences in transgenic resistance strategies. D3 discloses transgenic plants with enhanced resistance to powdery mildew comprising a MAP kinase substrate transgene. Hence the features mentioned

do not represent special technical features providing a common contribution over the state of the art shared by the whole claimed subject matter within the meaning of Rule 13.2 PCT.

In the light of the state of the art there are two problems underlying the present application. Firstly the provision of plants with enhanced disease resistance and secondly the detection of increased expression in transgenic plants of a polypeptide of the type identified in SEQ ID NO:2. The solutions are respectively the introduction of MAP kinase substrates with the structural characteristics identified in the claims e.g. SEQ ID NO:2 into plants by transformation, and the use of antibodies to detect the MAP kinase substrate polypeptide in a protein extract derived from the transgenic plant. No further special technical features linking the solutions or the problems can be identified, hence there is no single inventive concept underlying the claimed inventions within the meaning of Rule 13.1 PCT. Consequently there is a lack of unity and the different claimed inventions not belonging to a common inventive concept have been formulated as different subject matters as follows

1. Claims 1-18,23-26:Transgenic plants comprising a nucleic acid encoding a MAP kinase substrate 1 (MKS1) represented by the sequences defined in the claims and methods for producing the plants.

2. Claims 19-22: Method for the detection of MKS1 polypeptide - reacting an anti-MKS1 antibody with a protein extract from a plant. Anti-MKS1 antibody - polyclonal and monoclonal.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

5 **Novelty**

5.1 The subject matter of claims 1-18,24 and 26 is not new within the meaning of Article 33(2) PCT for the following reasons.

5.2 D1(cf. SEQ ID NOS:49381 and 49382 encoded by 49380) discloses a sequence identical with SEQ ID NO:2 i.e a MKS1 polypeptide. It also claims transgenic plants comprising this sequence(cf. claims).Consequently enhanced disease resistance is an inherent property of these plants. Methods and vectors for producing the transgenic plants is also implicitly disclosed The subject matter of claims 1,15,18,24 and 26 therefore not new.

5.2.1 The subject matter of claims 2-14,16, and 17 does not add new subject matter over that of the claims mentioned in 5.2 as the claimed combination of features is also made available by D1.

6 Inventive Step

6.1 The requirements of Article 33(3) PCT are not fulfilled, as even if novelty can be (re)established for the subject matter underlying claims 1-18, and 23-26 it would lack an inventive step for the following reasons.

6.2 The closest state of the art is D4. It discloses transgenic plants overexpressing the substrate of MPK4 having enhanced disease resistance. The disclosure is not enabling in that MKS1 is not made available. The subject matter of the application differs from that of D4 in that it identifies the substrate MKS1. The problem underlying the application is the implementation of the concept made available in D4. In view of the need to develop effective disease resistance in plants there is an incentive from D4 to reduce the teaching thereof to practice. D5 is in the field of disease resistance in relation to MPK4 and discloses the means by which to identify the substrate (MKS1). The skilled person would be aware of this teaching. Since the application of this teaching provides the skilled person with a reasonable expectation of solving the problem, the claimed subject matter would be arrived at in an obvious manner devoid of inventive skill or ability.

Re Item VIII

Certain observations on the international application

7 Clarity

7.1 In order to expedite the procedure the division notes the following deficiencies arising from the requirements of Article 6 PCT.

7.2 It is not clear if **MAP kinase substrate** refers to a MAP kinase that is a substrate, or to a substrate for a MAP kinase. In the latter case this does not appear to be limited to a substrate of MPK4. However the application is only directed to substrates of this kinase. This inconsistency leads to a lack of clarity and an absence of the essential technical features. The term **MKS1** is a laboratory designation without any technical meaning. The technical feature associated with the term **conservatively substituted** is unclear since the term does not have an unequivocal meaning.

7.3 Claims 24 and 26 refer to a product defined by a process of manufacture. This is only allowed in the case that the plant may not more precisely defined. As such the claims lack the essential technical features of the invention.